Pancreas

D’Onofrio Mirko\textsuperscript{1}, Vullierme Marie-Pierre\textsuperscript{2}, Válek Vlastimil\textsuperscript{3}, Principe Francesco\textsuperscript{1}, Canestrini Stefano\textsuperscript{1}, Gallotti Anna\textsuperscript{1}, Pozzi Mucelli Roberto\textsuperscript{1}

\textsuperscript{1}Department of Radiology, GB Rossi University Hospital, Verona, Italy; \textsuperscript{2}Department of Radiology, Beaujon Hospital, Paris, France; \textsuperscript{3}Department of Radiology, Brno University Hospital, Czech Republic.
Content

Topographic Remarks ................................................................. 2
Pancreas anatomy ........................................................................ 2
  Pancreatic and peripancreatic veins .................................... 3
  Pancreatic and peripancreatic arteries ................................. 3
  Pancreatic ductal system ....................................................... 3
  Pancreas development .......................................................... 4
US study of the pancreas and anatomy .................................... 4
Doppler study of the pancreas and vascular anatomy .......... 6
Pancreatic diffuse inflammatory disease ................................. 8
  Acute pancreatitis ............................................................... 8
  Chronic pancreatitis .......................................................... 9
  Autoimmune pancreatitis ................................................. 10
Pancreatic focal inflammatory disease .................................... 12
  Mass-forming pancreatitis ............................................... 12
  Pseudocyst ...................................................................... 12
Pancreatic solid neoplasm ...................................................... 13
  Ductal adenocarcinoma ..................................................... 13
  Endocrine tumors ........................................................... 14
  Lymphoma ..................................................................... 16
  Metastases ...................................................................... 16
Pancreatic cystic neoplasm ...................................................... 16
  Serous cystadenoma ........................................................ 16
  Mucin producing neoplasms ............................................. 17
  Mucinous cystoadenoma .................................................. 17
  Mucinous cystoadenocarcinoma ....................................... 18
  IPMN ............................................................................. 19
References ............................................................................... 19

Topographic Remarks

The pancreas is a medium retroperitoneal organ, slightly flattened and tapered, located transversally in front of the main vessels, at the level of the first or second lumbar vertebra. It has to be considered a quite fixed posterior organ.
It presents a slightly oblique shape extending left-upward, with the cephalic portion generally in a lower position compared to the body and the tail. It lies against the vertebral column, which determines a slight curvature of the organ, and is surrounded by soft retroperitoneal and peritoneal tissue.

Pancreas anatomy

The pancreas is a compound racemose gland, which exocrine excretion of is represented by the pancreatic juice, an important digestive fluid, while the endocrine secretion consists of enzymes involved in sugar metabolism.
The pancreas is usually divided in four parts: head, with the uncinate process, neck, body and tail.
The head lies within the curve of the duodenum and appears completely leaned against the posterior abdominal wall in contact with the inferior vena cava behind and the portal vein at the top. 

The uncinate process originates from the lower left portion of the head and lies posteriorly to the superior mesenteric vessels. 

The neck or isthmus generally appears as a slight constriction connecting the head to the body. It is located in front of the superior mesenteric vein and completely overlaid on its anterior surface by the posterior parietal peritoneum; its postero-inferior surface is related to the origin of the portal vein, formed by the junction of the superior mesenteric and splenic veins. 

The body appears leaned against the posterior abdominal wall by the white line of Toldt. Here the posterior parietal peritoneum, which overlays the front face of the pancreatic body, limits the posterior face of the epiploon retrocavity. The pancreatic body is frontally covered by the gastric cavity while posteriorly is in contact with the splenic vein; moreover it is related with the superior mesenteric artery and the left renal vein, which courses between the superior mesenteric artery and the aorta to merge into the inferior vena cava. The superior margin is slightly anteriorly crossed by the splenic artery, which arises from the celiac artery, whereas the inferior margin lies upon the duodenojejunal flexure. 

The tail is quite posteriorly orientated, left-upward, getting in touch with the splenic hilum as well as the left adrenal gland and upper kidney. It represents the mobile part of the gland and, similarly to the body, is separated from the stomach by the epiploon retrocavity.

The anteroposterior dimension of the pancreas varies greatly among individuals and tends to decrease with the age. The indicative measurements are: head 2 cm; neck < 1 cm; body and tail 1-2 cm, whereas the mean length is 13-15 cm [(1)].

**Pancreatic and peripancreatic veins**

The veins of the pancreas open into the splenic and superior mesenteric veins, from which junction the portal vein originates. 

The superior mesenteric vein runs over the uncinate process, whereas the splenic vein, rising from the splenic hilum, courses along the supero-posterior surface of the pancreas.

**Pancreatic and peripancreatic arteries**

The arteries of the pancreas derive from the splenic and the pancreaticoduodenal branches of the hepatic and superior mesenteric arteries. 

The splenic artery, arising from the celiac artery, runs along the superior margin of the gland. From it, some arteries perpendicular to the splenic artery, enter the body’s and tail’s parenchyma. In 92% of cases also the common hepatic artery, which courses along the superior margin of first portion of the duodenum and continues into the proper hepatic and gastroduodenal arteries, arises from the celiac artery [(2)]. The gastroduodenal artery courses along its ventral surface. 

The superior mesenteric artery, arising from the aorta behind the lower portion of the pancreatic body, courses anteriorly to the uncinate process and the third portion of the duodenum.

**Pancreatic ductal system**

The pancreatic ductal system is represented by the main pancreatic duct (Wirsung’s duct) and the accessory, functional or not, pancreatic duct (Santorini’s duct).
The main pancreatic duct takes origin from the junction of the small ducts of the tail lobules. It ranges transversely from the left to the right through the substance of the pancreatic body to flow into the major duodenal papilla (of Vater) jointly with the common bile duct. It appears as a thin hypoechoic line bordered by two echogenic margins and its diameter varies from a maximum of 3 mm in young adults to 5 mm in the elderly. The common bile duct, crossing the anterior surface of the portal vein to the right of the proper hepatic artery, runs behind the first portion of the duodenum to arrive into the parenchyma of the pancreatic head, close to the second portion of the duodenum.

The accessory pancreatic duct (Santorini’s duct) originates from the duct of Wirsung and crosses just the head of the pancreas, more superficially than to the main duct, to flow into the minor duodenal papilla, 2 cm higher than the major one.

**Pancreas development**

The pancreas develops in two parts, the dorsal and the ventral. The dorsal part arises as a diverticulum from the dorsal side of the duodenum, just above the hepatic digression and, growing upward and backward into the dorsal mesogastrium, forms a part of the head and the uncinate process as well as body and tail as a whole.

The ventral portion appears as a diverticulum from the primitive bile-duct, forming the remaining part of the head and the uncinate process. As a consequence the duct of the dorsal part (accessory pancreatic duct) opens independently into the duodenum, while the duct of the ventral part (main pancreatic duct) opens together with the common bile-duct. Around the sixth week of gestation the two parts of the pancreas meet and fuse, establishing a communication between their ducts. After that, the terminal part of the accessory duct undergoes just a little enlargement and its opening into the duodenum is sometimes obliterated, whereas the pancreatic duct increases in size and forms the main duct of the gland.

At first the pancreas is directed upward and backward between the two layers of the dorsal mesogastrium, which give it a complete peritoneal sheath, its surfaces facing the right and the left side. With the change in the position of the stomach, the dorsal mesogastrium is drawn downward and to the left, so that the right side of the pancreas is directed backward and the left forward. The right surface ends connected to the posterior abdominal wall and the peritoneum covering it undergoes absorption; thus, in the adult, the gland appears to lie behind the peritoneal cavity.

**US study of the pancreas and anatomy**

The study of the pancreas includes transverse, longitudinal and angled oblique scan planes [Figure 1].
The plane passing through the emergency of the celiac trunk should identify the body-tail, in relation with the presence of gastric gas; the left portions of the gland result partially covered by bowel gas.

The plane passing through the splenic vein demonstrates the typical “comma” morphology, and by this scan is easily possible to evidence the body with the Wirsung’s duct [Figure 2] and the isthmus of the pancreas on the vein confluence of the splenic with the superior mesenteric.

At the level of the lateral border of the head are often seen ventrally the gastroduodenal artery, represented by anechoic image, and dorsally the common bile duct.

Figure 1  Pancreas. Ultrasound oblique scan of the pancreatic gland with visualization of the pancreatic tail, the body, the isthmus and the upper part of the head of the pancreas.

Figure 2  Wirsung’s duct. Ultrasound oblique scan of the pancreatic body with visualization of the main pancreatic duct (arrow).
The scan passing through the mesenteric vessels visualizes the lower portion of the pancreatic head and the uncinate process, anatomically located between the superior mesenteric vein and the inferior vena cava. Moreover the superior mesenteric artery appears in front of the aorta, to the left of the superior mesenteric vein. The longitudinal scans are executed on the four anatomic parts of the pancreas. The head is visualized in all its extension, as well as its relationship with the inferior vena cava. Its cephalic portion is cranially delimited by the portal vein and the first duodenal part; more caudally it relates with the third duodenal portion. By a longitudinal and slightly oblique scan is usually possible to visualize the intra-pancreatic common bile duct [Figure 3].

**Figure 3**  Intrapancreatic common bile duct. Ultrasound longitudinal and slightly oblique scan of the pancreatic head with visualization of the Wirsung’s duct and the intrapancreatic tract of the common bile duct (arrow).

The scans at the neck level need the superior mesenteric vein as reference point; it is visualizable up to the junction with the splenic vein. Just more dorsally is possible to recognize the uncinate process. The Wirsung’s duct can be visualized at the level of the pancreatic body [Figure 2]. The reference point on the body is represented by the splenic vessels, transversally orientated, which course on the superior border. The tail can be visualized by a longitudinal anterior scan, even if the demonstration of this anatomic structure is often difficult, owing to the gastric gas covering. The left intercostal scans are generally used to localize the caudal portion by using the splenic acustic window.

**Doppler study of the pancreas and vascular anatomy**

Doppler studies are an integral part of ultrasound examination of the pancreas [(3)](3). The peripancreatic vascular structures evaluated and well recognized are the portal vein, the tripod trunk, the splenic artery and vein, the gastroduodenal artery, the superior mesenteric artery and vein, the aorta and the inferior vena cava; whereas just a few parenchymal vessels are usually appreciable in normal conditions. However the visualization of smaller
peripancreatic [Figure 4] and intrapancreatic [Figure 5] vessels is possible thanks to the increased Doppler sensitivity.

**Figure 4** Gastroduodenal artery. Color-Doppler ultrasound longitudinal scan of the pancreatic head with the visualization of the gastroduodenal artery.

![Figure 4](image)

**Figure 5** Pancreatic arterial arcades. Power-Doppler ultrasound transversal scan of the pancreatic head with the visualization of the pancreatic arterial arcades.

![Figure 5](image)

Clinical applications of the Doppler studies of peripancreatic vessels include the assessment of patency and features of blood flow. Doppler and pulsed-Doppler appearance of peripancreatic vessels has been well documented [(1;2)]. In normal conditions, the mean speed of blood in peripancreatic arteries is about $103 \pm 18$ cm/s in the celiac trunk, $78 \pm 16$ cm/s in the hepatic artery, $85 \pm 18$ cm/s in the splenic artery and $100 \pm 22$ cm/s in the superior mesenteric artery [(1)]. Mean portal flow velocity is
12-20 cm/s. The resistance index in the superior mesenteric artery is in general higher than in the other arterial vessels [(1)]. Abnormal signals and physiological variations in Doppler waveform in peripancreatic vessels are not quite understood, because of the influence of physiologic, pharmacologic and pathological conditions [(1)]. However, Doppler examination allows recognizing the changes produced by diseases in peripancreatic vessels.

**Pancreatic diffuse inflammatory disease**

**Acute pancreatitis**

Acute pancreatitis is an acute inflammatory process that may include suppurative, necrosis and hemorrhage of pancreatic tissue, with variable involvement of other regional and remote tissues. Diagnosis is usually based on the laboratory assay of serum amylase and lipase levels [(3)]. Acute pancreatitis is classified as mild (interstitial edema) [Figure 6] or severe (necrosis, fluid collections) [Figure 7]. Biliary stones can be detected at the time of the diagnosis. Peripancreatic collections [Figure 7] and then pseudocysts follow the different timing of the disease.

**Figure 6** Mild acute pancreatitis. Ultrasound oblique scan of the pancreatic gland shows enlargement of the gland with the body appearing slightly hypoechoic in respect to the head.
Normal US findings can be seen in patients with mild acute pancreatitis. Although the pancreas can appear normal in acute pancreatitis, the most frequent findings are focal or diffuse enlargement of the gland with a decrease of normal echogenicity [Figure 6]. The pancreas is seen as more hypoechoic than the liver and the pancreatic texture may also appear heterogeneous. Acute pancreatitis can be focal or diffuse, depending on its distribution [(4)]. At contrast-enhanced ultrasound (CEUS) the pancreatic segment involved by mild acute pancreatitis shows an increased contrast enhancement due to hyperemia. Severe acute pancreatitis is characterized by the presence of large confluent necrotic areas and CEUS may improve the identification and delimitation of these necrotic areas, which appear as avascular at dynamic imaging [(5;6)].

**Chronic pancreatitis**

Chronic pancreatitis is an inflammatory disease characterized by the replacement of the pancreatic glandular elements by fibrous tissue. It is clinically characterized by a progressive pancreatic functional loss [(7)]. Although early morphologic changes of chronic pancreatitis are difficult to recognize at imaging, the findings of advanced disease are readily detected. Alterations in size of the pancreas may be seen in fewer than half of patients affected by chronic pancreatitis [(8-10)]. Atrophy and focal alterations in pancreatic size are the most easily identified changes, expression of advanced stages. The glandular contours appear irregular, sharp and sometimes lumpy.

Echogenicity of the pancreas is usually increased in chronic pancreatitis due to adipose infiltration [(11)] and fibrosis [(12-14)]. However since the presence in elderly and obese subjects, it is not a specific parameter. Parenchymal echo structure alteration, on the other hand, is a more specific sign of chronic pancreatitis. The pancreatic echotexture is inhomogeneous and coarse due to the coexistence of hyperechoic and hypoechoic foci, fibrosis and inflammation signs respectively [(12;14)]. These findings are described in 50%-70% of cases [(9;10)]. In patients affected by severe exocrine pancreatic insufficiency this percentage increases to about 80% [(8)], therefore showing the fairly good sensitivity of this finding. Apparent normality of the glandular echotexture in chronic pancreatitis is reported in the literature in up to 40% of cases and expected especially in the early stages of the disease.
However, state-of-the-art US imaging has good capabilities for identifying the fine alterations of glandular texture present in the early stages of the disease, making the evaluation of pancreatic echostructural alterations an important finding for diagnosis. The most important diagnostic criterion for chronic pancreatitis is the presence of pancreatic calcifications [(18)], whose identification is pathognomonic. Caliber abnormalities in chronic pancreatitis are essentially represented by main pancreatic duct dilation. Wirsung’s duct can be considered dilated when its caliber is larger than 3 mm [(14)], with a sensitivity of about 60%–70% [(10;11)] and a specificity, of about 80%–90% [(10;19;20)]. The limits of the reported sensitivity reflect the minor frequency of duct dilation in initial and/or light cases of chronic pancreatitis. In the early phases of chronic pancreatitis the Wirsung duct may have a normal diameter [(12)]. Moreover, compression of the main pancreatic duct may lead to secondary obstructive chronic pancreatitis upstream of the obstacle, with the same pathogenetic mechanism. Solid and cystic lesions may cause duct compression (benign) or infiltration (malignant) if contiguous to the main pancreatic duct, with progressive development of obstructive chronic pancreatitis upstream [(11)]. Therefore the most significant US findings in chronic pancreatitis are pancreatic duct dilation and intraductal calcifications [Figure 8].

**Figure 8** Chronic pancreatitis. Ultrasound oblique scan of the pancreatic glad shows main pancreatic duct dilation and calcifications.

**Autoimmune pancreatitis**

Autoimmune pancreatitis is a particular type of chronic pancreatitis, with a very recent pathological definition. It is characterized by periductal inflammation, mainly substained by lymphocytic infiltration, with evolution to fibrosis. As opposed to the other forms of chronic pancreatitis, the pancreas is increased in volume, usually in a diffused way with the typical “sausage” aspect and the Wirsung duct is compressed or string-like [(21)]. US features include reduced echogenicity of the gland, diffuse or focal pancreatic enlargement, absence of any fluid collection or calcification. US findings are typical in the diffuse form when the entire gland is involved [Figure 9a]. The Wirsung’s duct is compressed by glandular inflamed parenchyma. The overall sensitivity of US in the diagnosis of chronic pancreatitis is variable, with an average range in most series of 60%–70% [(7;8)].
Figure 9  Autoimmune pancreatitis. a) Ultrasound oblique scan of the pancreatic gland shows diffuse enlargement of the gland with the typical “sausage” aspect in absence of any fluid collection or calcification. b) at CEUS diffuse moderate enhancement is visible.

CEUS of autoimmune pancreatitis shows moderate diffuse enhancement in the early contrast-enhanced phase, though inhomogeneous [Figure 9b]. Contrast medium washout is usually slow but progressive. CEUS findings may be especially useful in the study of focal forms of autoimmune chronic pancreatitis, in which differential diagnosis with ductal adenocarcinoma is a priority [(22)]. Autoimmune chronic pancreatitis shows a remarkable response to steroid therapy because of its autoimmune pathogenesis [(23;24)].
**Pancreatic focal inflammatory disease**

**Mass-forming pancreatitis**

Mass-forming chronic pancreatitis usually occurs in patients with a history of chronic pancreatitis [(25)] and must be differentiated from pancreatic ductal adenocarcinoma. At CEUS, a mass-forming chronic pancreatitis shows a “parenchymographic” enhancement, characterized by an enhancement pattern always comparable to that of the surrounding pancreatic parenchyma. However, in long-standing chronic inflammatory processes, inhomogeneous hypovascularization of the lesion may be observed, probably owing to the presence of a large amount of fibrosis and the differential diagnosis becomes more difficult [(5;26;27)].

**Pseudocyst**

Pseudocysts can be a complication of severe acute pancreatitis [Figure 10] or can occur in chronic pancreatitis [(22)]. Characterized by a fibrous wall without an epithelial lining [(28)], pseudocysts must be differentiated from pancreatic cystic tumors, especially mucinous cystadenomas (MCAs), as they require completely different therapeutic approaches [(28)]. CEUS has a crucial role in differential diagnosis of pseudocysts and pancreatic cystic tumors, better evaluating the micro-vascularization of the intralesional inclusions.

**Figure 10**  Pseudocyst. Ultrasound oblique scan of the pancreatic body shows huge rounded cystic lesion after severe acute pancreatitis.

![Image](ultrasound-pancreas.jpg)

Even if characterized by an inhomogeneous content at conventional US, all the inclusions in pseudocysts are always completely avascular, becoming homogeneously anechoic during CEUS examination [(26)].
Pancreatic solid neoplasm

Ductal adenocarcinoma

About 90% of pancreatic tumors are ductal adenocarcinomas. They’re composed of infiltrating epithelium resuming ductal structures. In almost two thirds of patients with pancreatic adenocarcinoma, the tumor is located in the head of the pancreas; while involves the body and/or the tail, or diffusely infiltrates the entire gland in the rest of them. Macroscopically, ductal adenocarcinoma appears as schirrous infiltrating mass [(29-32)]. Masses in the head of the pancreas cause a ductal obstruction with secondary dilation of both the common bile duct and the pancreatic duct, resulting in the so-called “double-duct sign”. However this presentation can also be present in the case of chronic pancreatitis. In particularly aggressive forms of adenocarcinoma the development of necrosis or colliquation is common, resulting from the difference between the growth rate and the formation of microvessels by angiogenesis. The necrotic/fluid part of the tumor is mainly located centrally. A ductal adenocarcinoma is characterized by infiltrative margins with diffusion to the tumor to the adjacent parenchyma and structures. This feature could explain the common lack of clear-cut margins during examinations. More frequently, at US, the adenocarcinoma appears hypoechoic to the adjacent pancreatic parenchyma [Figure 11].

Figure 11  Ductal adenocarcinoma. Ultrasound oblique scan of the pancreatic body shows hypoechoic mass with ill-defined infiltrative margins and upstream main pancreatic duct dilation.

The main pancreatic duct is usually infiltrated and upstream dilated. Doppler studies show poor or no vascularity inside the lesion. The vascular invasion is defined by a focal absence of the echogenic interface of the vessel wall, or by a narrow lumen, with changes in blood flow velocity [(33-35)]. Principal criteria of unresectable pancreatic cancer are liver or peritoneal metastases and invasion of major peripancreatic vessels [(36)]. At CEUS, ductal adenocarcinoma enhancement is poor in all contrast-enhanced phases [Figure 12].
Figure 12  Ductal adenocarcinoma. Contrast-enhanced ultrasound transversal scan of the pancreatic head showing a markedly hypovascularized mass with upstream main pancreatic duct dilation.

The margins and size of the lesion are more clearly visible. The depiction of tumoral margins at CEUS is more accurate at a low enhancement of pancreatic adenocarcinoma [(37)], because in cases of well-differentiated lesions the mass tends to be isovascular compared to the remaining parenchyma and the margins of the tumor are no longer visualized. Relationship with peripancreatic arterial and venous vessels can also be evaluated for local staging [(26;27;37;38)].

The degree of tumoral differentiation of the adenocarcinoma influences the microvascular density [(26;27;37;38)]. Moreover, the pattern of enhancement of pancreatic adenocarcinoma influences the depiction of tumoral margins at CEUS [(37)].

After studying a pancreatic lesion during the arterial, pancreatic and venous phases, the presence of liver metastases have to be excluded during the late phase [(26)].

Since US often represents the first technique performed, the use of CEUS will improve the diagnostic accuracy when a focal hypoechoic solid lesion has been detected.

Endocrine tumors

Pancreatic endocrine tumors or islet cell tumors arise from the neuroendocrine cells of the pancreas. These tumors are classified as functioning or nonfunctioning, based on the presence or not of symptoms related to hormone production. Insulinomas and gastrinomas are the most common functioning islet cell tumors and they are usually small at the time of diagnosis. The other functioning neuroendocrine tumors (vipoma, glucagonoma and somatostatinoma) are rare, account for about 20% of functioning neuroendocrine tumors of the pancreas [(39;40)].

Nonfunctioning tumors are frequently large at diagnosis [Figure 13a] and often malignant [(41)].

Figure 13  Endocrine tumor (nonfunctioning). a) Ultrasound transversal scan of the pancreatic head shows large hypoechoic mass with well-defined margins and upstream main pancreatic duct dilation. b) the lesion is hypervascular at contrast-enhanced ultrasound.
Insulinomas are usually benign and solitary pancreatic lesions, while gastrinomas tend to be malignant and multiple.
Insulinomas represent the most frequently found functioning neuroendocrine tumors of the pancreas (about 60% of all neuroendocrine tumors), benign (85%–99%) and single (93%–98%) [(42;43)] in the majority of cases. Insulinoma appears as hypoechoic pancreatic nodules, usually capsulated.
At the time of clinical presentation 50% of the tumors are smaller than 1.5 cm [(40)]. When malignant their diameter is generally >3 cm and about a third of these have metastases at the time of diagnosis [(42;43)]. The mean diameter of insulinomas is <15 mm, while gastrinomas are usually larger [(39)].
Gastrinomas are the second most frequently found functioning neuroendocrine tumors of the pancreas (about 20% of all neuroendocrine tumors) [(39;40)].
These tumors differ from insulinomas in localization and size [(39;44;45)]. They occur within the gastrinoma triangle (junction of the cystic duct and common bile duct–junction of the second and third parts of the duodenum–junction of the head and neck of the pancreas), of
which only the pancreatic side is correctly explorable by US [(39;40)]. Identification of pancreatic gastrinomas can be easy considering their moderate size [(40;45)]. Liver metastatic lesions are present in 60% of cases at the time of diagnosis [(40;46)]. Nonfunctioning islet cell tumors represent up to 33% of neuroendocrine tumors of the pancreas [(47)], ranging from 1 to 20 cm in diameter and showing a high malignancy rate, up to 90% [(47;48)]. However they are less aggressive than adenocarcinomas. These tumors, characterized by predominantly expansive growth, are not clinically apparent until adjacent viscera and structures have become involved. At US they appear well margined and usually easy to detect, thanks to their size. Due to their dimensions, necrosis and hemorrhage can be present, developing a typical inhomogeneous appearance, sometimes accompanied by very small intralesional calcifications. Larger nonfunctioning islet cell tumors show cystic degeneration or cystic changes [(39)]. The finding of numerous intratumoral vascular spots is typical of neuroendocrine pancreatic tumors at color-Doppler. In particular, a “spot” pattern can be demonstrated in both large and small endocrine tumors [(39)]. However, while positive Doppler results predict hypervascularization of the lesion, a Doppler “silence” can also be present in hypervascular endocrine tumors because of the small size of the tumoral vascular network.

At CEUS, different enhancement patterns can be observed in relation to the size of tumors and tumoral vessels. Voluminous endocrine tumors show a rapid and intense enhancement in the early contrast-enhanced phase [Figure 13b], with the exception of necrotic intralesional areas [(39;49;50). In moderate-sized neuroendocrine pancreatic tumors, a capillary blush enhancement can be present in the early contrast-enhanced phase, then becoming hypoechoic in the late contrast-enhanced phase [(39;49;50). Nonfunctioning neuroendocrine tumors can also be hypovascularized, depending on the amount of stroma inside the lesion which is dense and hyalinized [(22)].

**Lymphoma**

Pancreatic lymphoma is represented by the non-Hodgkin B-cell histotype and usually associated with lymph nodes or lesions in other organs. US shows focal or diffuse pancreatic enlargement, hypoechoic relative to the normal pancreatic parenchyma. [(36)]

**Metastases**

Pancreatic metastases are rare. Primary tumors that most frequently metastasize to the pancreas are from lung, breast, kidney and the melanoma [(51)]. Pancreatic metastases can appear as focal or multifocal, often as well demarcated lesions in patients with a known primary neoplasm. [(36)].

CEUS may well demonstrate the enhancement of pancreatic metastases from renal cell carcinoma, as they are clearly hypervascular, allowing differential diagnosis against ductal adenocarcinoma. However, their features cannot be differentiated from that of endocrine tumors and the differential diagnosis is therefore based on the clinical history and symptoms and finally on cytology [(52;53)].

**Pancreatic cystic neoplasm**

**Serous cystadenoma**

Serous cystadenoma (SCA) is a benign lesion. It is usually located in the head of the pancreas and generally characterized by tiny cysts of <20 mm [(54)]. The content of the cysts is a
glycogen-rich serous, transonic at US. If extremely microcystic SCA can have a solid appearance at US and CT.

In up to 15% of cases, the tumor contains a central scar, which may calcify. US imaging can show the microcystic appearance of this lesion related to the sponge macroscopic aspect. The central scar, if present, is often visible as a central solid echogenic portion of the tumor, sometimes containing calcifications. The contours of the SCA are always quite sinuous and the wall is thin. The internal septa normally are well orientated and centrally directed, reaching the central scar with a definitive typical aspect of the skeleton of this cystic lesion. Numerous thin septa with a radial arrangement give to the lesion its typical microcystic aspect.

SCAs do not communicate with the main pancreatic duct. The demonstration of that is fundamental, especially when the lesion is large, because it might compress the main pancreatic duct, so upstream dilated [36].

At CEUS, intrallesional septa enhancement improves the identification of the microcystic features of the lesion. The less common oligocystic or macrocystic types of serous cystadenoma present features indistinguishable from those of the other macrocystic tumors of the pancreas [(55;56)].

**Mucin producing neoplasms**

Mucin producing neoplasms of the pancreas may originate either from the peripheral ducts (mucinous cystic tumors) or from the main pancreatic duct and its collateral branches (intraductal papillary mucinous neoplasms; IPMNs) [(57)].

**Mucinous cystoadenoma**

Mucinous cystic neoplasm is a potentially malignant lesion. It is most often located in the body or tail of the pancreas in middle-aged women. The content of the cyst is mucin. At US, it appears as round or ovoid, usually unilocular lesion with thick wall and septa and occasionally peripheral calcifications. The mucinous content is viscous and may generate fine echoes in the internal part of the lesion that covers the internal wall of the cystic tumor and may Hale the inclusion such as internal septa and/or solid papillary projections. The number and the thickness of intrallesional septa and nodules are not always related to the grade of malignancy. Mucinous tumors may spread, involve lymph nodes and produce liver metastases [(58;59)].

CEUS may significantly improve the ultrasonographic detection of parietal nodules. The vascularization of septa and nodules can be demonstrated beaming hyperechoic [Figure 14], standing out against the lesional background, anechoic during the dynamic imaging. Therefore CEUS examination improves ultrasonographic differential diagnosis between MCA and pseudocyst, thanks to the identification and study of inclusions vascularization in cystic masses of the pancreas [(60)].
Figure 14  Mucinous cystadenoma. Ultrasound oblique scan of the pancreatic body shows rounded cystic mass with small enhancing septa.

Mucinous cystoadenocarcinoma
Mucinous cystoadenocarcinoma represents the malignant neoplastic transformation of mucinous cystoadenoma. Compared to the latter it is characterized by thicker wall and septa, disomogeneous content and a greater number of nodules [Figure 15], whose significant cell proliferation is responsible for wall and then peripheral structures invasion, leading to lymph nodes involvement and liver metastases development [(58;59)].

Figure 15  Mucinous cystadenocarcinoma. Ultrasound oblique scan of the pancreatic body shows huge rounded cystic mass with thick wall and several enhancing septa and nodules.
IPMN

Intraductal papillary mucinous neoplasm (IPMN) is recognized as a dilation of the main pancreatic duct and/or its branches or cyst formation with proliferation of pancreatic ductal epithelium and excessive production of mucin. IPMNs are classified into the main duct type, branch duct type, or a combination of the two [(61)]. The main duct type can be localized or diffuse. The localized main duct type of IPMN is characterized by highly inhomogeneous masses, related to neoplastic intraductal proliferation, with upstream dilation of the main pancreatic duct. The diffuse main type may be difficult to distinguish from chronic pancreatitis.

The branch duct mucinous tumor is characterized by cystic ectasia of one or more branches, forming masses. At US examination the mucin of IPMN, especially the ductectatic mucin-hypersecreting variant of the branch ducts, may not be easily differentiated from the solid portions of the tumor, which can therefore be mistakenly reported as solid. Harmonic imaging, with its better contrast resolution [(62;63)], may lead to better identify the non solid part of the lesion, thanks to the demonstration of more or less sharp intralesional interfaces. However, at US, final diagnosis of IPMN by demonstrating the communication with the pancreatic duct is difficult [(64)].

CEUS examination of the IPMNs may allow identification of intraductal papillary tumoral vegetations, especially in the papillary-villous variant, demonstrating its vascularization. CEUS can be a safe method to follow-up the border-line lesions evaluating changes in dimensions and vascularization of the inclusion. Considering that, in this setting, CEUS has the great advantage of being a noninvasive and low-cost technique [(55)].

References


